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Left Ventricular Hypertrophy (LVH) in different Stages of Chronic Kidney Disease (CKD) Patients and its Correlation with Anaemia

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Abstract:

Background : ***Chronic kidney disease (CKD) is a public health problem that increases the risk of cardiovascular morbidity and mortality. Heart failure with preserved ejection fraction characterized by left ventricular hypertrophy (LVH) and diastolic dysfunction is a common cardiovascular complication of CKD. Anaemia is present in both dialysis & non dialysis CKD patients. Anaemia causes left ventricular hypertrophy (LVH) which in turn leads to increases morbidity and mortality in CKD, even before progression of chronic kidney disease (CKD) to end stage renal disease (ESRD). Our study is aimed at to evaluate the prevalence of left ventricular hypertrophy (LVH) and its correlation with anaemia in hospitalized CKD patients.***

Materials and Methods : ***A cross-sectional study was done on 50 patients of different stages of CKD admitted in the chittagong medical college hospital (CMCH). All the clinical data were reviewed and recorded. Data was analyzed by SPSS-18 and p value <0.05 was considered statistically significant.***

Results : ***Majority of study population 64% was male, 36% was female. Most of the male patient (40%) of the study population were having abnormal left ventricular mass index (>130 gm/m^2). More patients with severe left ventricular hypertrophy were found in stage 5 of CKD in female and male which was 8 and 23 respectively. Regarding correlation of Hb% with LVMI there was a significant negative correlation was found (r= -0.420, p = 0.003) between them means if Hb% decreases LVMI level increases. It was also found in male and female patients separately (for male r = -0.778, p = 0.001 and for female r = -0.746, p = 0.001).***

Conclusion : ***Anemia is widely prevalent in our CKD patients. Severity of anemia is correlated to left ventricular hypertrophy in these patients. Hence correction of anemia early in these group of patients can halt or prevent cardiovascular morbidity and mortality.***

Key Words : ***Left ventricular hypertrophy (LVH), Anaemia, Chronic kidney disease, Stage of CKD.***

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Introduction :

The prevalence of cardiovascular disease in patients with CKD at all stages is higher than that of the general population. Cardiovascular disease including coronary artery disease, left ventricular hypertrophy, heart failure is common in patients with chronic kidney disease (CKD). Careful review of the literature in patients with kidney disease, reveals a high prevalence of LVH, in association with risk factors attributable to failing kidney function : hypertension, anaemia, and in some instances, abnormalities of mineral metabolism. It appears that LV growth occurs early in the course of kidney disease and is associated with modifiable risk factors, in particular a fall in hemoglobin. Left ventricular hypertrophy (LVH) is a cardiovascular complication highly prevalent in patients with chronic kidney disease (CKD) and end stage renal disease. Cardiovascular diseases are the leading cause of death among patients with chronic kidney disease as the risk of cardiovascular diseases increases in CKD patients, particularly among patients with end-stage renal failure (ESRD).[1] A significant association between the Glomerular filtration rate (GFR) and CVDs has been observed, as the decreasing GFR is considered a predictive factor for the development of CVD'S.[2] Various epidemiological studies have shown a paramount association between decreasing renal function and with ultimate outcomes of CVD's and mortality.[1] According to the statistics, the prevalence of CKD-associated cardiovascular diseases in the United Kingdom (UK) and the United States (US) was found to be 47.2% and 33.4% respectively.[1]

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Studies have investigated various pre-existing factors like hypertension, diabetes mellitus, anemia, and dyslipidemia as the causative factors for an increased incidence of CKD-induced cardiovascular diseases.[3] Hypertension is considered a powerful independent risk factor for CVD development, however, its association with CKD potentiates the hypertension impact on the cardiovascular system through the utilization of the renin-angiotensin system.[4] Left ventricular hypertrophy (LVH) is the most common structural abnormality associated with CKD patients accounting for 70% of the patients suffering LVH with ESRD.[5]

LVH emerges as an adaptive response to overload, such as pressure or volume, to some extent, but long term LVH leads to left ventricular dysfunction, resulting in the constriction of the renal arteries , less blood perfusion of the glomeruli, and alteration of the glomerular membrane filtration coefficient and tubular reabsorption. The inflammatory response associated with LVH also contributes to the progression of CKD.[6]

The association of anemia with chronic kidney disease (CKD) has been recognized since the early 19th century. Moreover, various studies done over the years have shown not only a higher incidence of anemia, but also a significantly higher incidence of cardiac complications, particularly left ventricular hypertrophy in chronic kidney disease patients.[7] In chronic kidney disease patients, various uremia related risk factors for cardiovascular disease includes anemia, hyperparathyroidism, abnormalities of mineral metabolism, acidosis, of note, association of anemia have been consistently described in all population of kidney disease. Anemia is defined as decrease in either percentage of RBC (hematocrit) or decrease in haemoglobin concentration in sample of venous blood when compared to reference values. In our study reference value is taken as 11 g/dl for both male and female. Anemia of renal failure mainly caused by lack of sufficient quantity of endogenous erythropoietin production, partially due to iron deficiency which can be attributed to increased demand due to increased erythropoesis in response to exogenous EPO, gastrointestinal bleed, ongoing blood loss with dialyzer and tubing and due to frequent sampling and venupuncture. Anemia has been cited as an independent risk factor for the development of left ventricular hypertrophy (left ventricular hypertrophy) in chronic kidney disease patients.[7] Anemia leads to hemodynamic as well as non hemodynamic adaptation. Non-hemodynamic adaptation includes increase in erythropoietin hormone and intraerythrocytic 2,3 DPG. Whereas hemodynamic adaptation takes place when Hb is <10 g/dl, includes increase cardiac preload and reduced SVR, both of which leads to high cardiac output, which if remains for long term leads to left ventricle remodelling (initial dilatation and subsequent hypertrophy). Left ventricular hypertrophy is premature CVD that develop rapidly during progression of chronic kidney disease and is strong indicator of mortality in patient with ESRD. It is known that anemia is a strong predictor of development of left ventricular hypertrophy and morbidity and mortality in ESRD. The importance of anemia in ESRD dialysis patients was shown by the observation that decreases in Hb level of 1 g/dl incrementally increased mortality by 18-25% and left ventricular hypertrophy by ~50%. In fact the role of anemia as a cardiac risk factor was shown in an evaluation of 246 patients in which it was found that every 0.5 g/dl decrease in Hb increased the relative risk of left ventricular growth by 32% (p=0.04).5 Also in a prospective study of recombinant erythropoietin use in pre-dialysis patients; increase in mean Hb of 2.7 g/dl was accompanied by a decrease in left ventricular mass index (left ventricular mass index) in almost all patients.[7] This even in the absence of improved blood pressure control, confirmed the role of anemia in the genesis of left ventricular hypertrophy.

Thus, the role of recombinant erythropoietin for correction of anemia which was shown to lead to the reversal of hypertrophy, came into significance. Thus, though heart disease is common in chronic kidney disease, not all cardiac disease in chronic kidney disease patients caused by conventional or atherosclerotic processes, nor due to ischemic changes. Instead, anemia is major independent risk factor for development of left ventricular hypertrophy in chronic kidney disease

patients. Being a modifiable risk factor, if anemia is treated by intervening early in disease course, left ventricular hypertrophy can be arrested or to some extent reversed. In the same context, the present study was carried out.

Therefore, this cross sectional study aimed at to estimate the prevalence of LVH in CKD patients.

Materials and Methods :

This cross sectional observation study done on 50 patients of different stages CKD admitted in the Nephrology Department of Chittagong Medical College Hospital. We included all the CKD patients of both sex, aged ≥18 years consecutively with feature of LVH in Echocardiography during the study period. But CKD with cardiomyopathy & valvular heart disease, CKD with haematological disease, CKD with chronic infectious disease, CKD with malignant condition were excluded. A preformed standard case record form was used for data collection. All clinical data including pattern of left ventricular mass index (LVMI), Relation of LVMI with different stages of CKD, Correlation of Hemoglobin level with LVMI among male & female patients were recorded.

CKD was defined as kidney damage or Glomerular filtration rate (GFR) of <90ml/min/1.73 m^2 for three months or more, irrespective of cause or evidence of kidney damage.[8] Stage of CKD is classified as stage 1, 2, 3, 4 & 5 based on GFR category (stage 1 : eGFR e"90, stage 2 : (60-89), stage 3 : (30-59), stage 4 : eGFR (15-29), stage 5 : eGFR <15.[9] Left ventricular hypertrophy was defined as LVMI >95 g/m^2 in females and >115 g/m^2 in males [10] as per the novel American Society of Echocardiography (ASE) criteria. Anaemia was defined as serum hemoglobin levels e" 12g/dl in women and e" 13gm/dl in men agee"18years old, as recommended by the National Anemia Action Council and theWorld Health Organization.[11] GFR: can be estimated from calibrated serum creatinine and estimating equations, such as the Cockcroft-Gault formula (normalized for the body surface area [BSA]): (140 - Age [years]) x weight (kg) x (0.86, if female) x 1.73/72 x serum creatinine (mg/dl) x BSA (m2) .[12]

ECG & Echocardiography were done by expert cardiologist in Cardiology department of CMCH. 10cc venous blood underwent for Hb% and PBF examination. Blood Urea and Serum creatinine were measured by Urease GLDH and Jaffe method respectively. Data were collected by interview and recording reports of laboratory investigations. All the collected data were checked and compiled and then tabulated. The data were entered into SPSS for Windows 18. All data were evaluated by using chi-square test for categorical variables and t-test for continuous variables. The results were presented in tables and figures. Statistical significance was set at $P < 0.05$.

Results:

Table 1 showing among 18 female > 112 LVMI was found in 10 (20%) patients , whereas in male >130 gm/m^2 was found in 20 (40%) of patients.

Table 2 showing more patients with severe LVH were found in stage 5 of CKD in female and male which was 8 and 23 respectively.

Table 3 showing regarding correlation of Hb% with LVMI there was a significant negative correlation was found (r= -0.420, p = 0.003) between them means if Hb% decreases LVMI level increases. It was also found in male and female patients separately (for male r = -0.778, p = 0.001 and for female r = -0.746, p = 0.001).

Table-I

Pattern of left ventricular mass index (LVMI).

(a): Left ventricular mass index (LVMI) in female

LVMI	Frequency	Percent
< 100 gm/m^2 (Mild)	2	4.0
101-112 gm/m^2 (Moderate)	6	12.0
>112 gm/m^2 (Severe)	10	20.0
Total	18	36

(b): Left Ventricular mass index (LVMI) in male

LVMI	Frequency	percent
< 116 gm/m^2 (Mild)	5	10.0
117-130 gm/m^2 (Moderate)	7	14.0
> 130 gm/m^2 (severe)	20	40.0
Total	32	64.0

Table-2

Relation of LVMI with different stages of CKD

Table 2a : LVMI grading for female with CKD stages

LVMI grading			Stage of CKD Stage 5	Stage 4	Stage 3
for female	<100gm/m^2	Count	0	0	1
		% within stage of CKD	0.0%	0.0%	14.3%
	101-112 gm /m^2	Count	1	1	5
		% within stage of CKD	11.1%	50.0%	71.4%
	>112gm/m^2	Count	8	1	1
		% within stage of CKD	88.9%	500.0%	14.3%
Total		Count	9	2	7
		% within stage of CKD	100.0%	100.0%	100.0%

Table 2b : LVMI grading for male with CKD stages

LVMI grading male			Stage 5	Stage 4	Stage 3
	<116 gm/m^2	Count	0	0	5
		% within stage of CKD	0.0%	0.0%	71.4%
	117-130 gm/m^2	Count	4	1	2
		% within stage of CKD	17.4%	50.0%	28.6%
	>130 gm/m^2	Count	19	1	0
		% within stage of CKD	82.6%	50.0%	0.0%
Total		Count	23	2	7
		% within stage of CKD	100.0%	100.0%	100.0%

Table-III

Correlation of Hemoglobin level with LVMI among male & female patients .

Table III (a) : Overall correlation of Hb% with LVMI

		Hb%	Echocardiography LVMI
Hb%	Pearson correlation	1	-0.420**
	Sig. (2-tailed)		0.003
	N	49	49
Echocardiography LVMI	Pearson correlation	-0.420**	1
	Sig. (2-tailed)	0.003	
	N	49	49

** Correlation is significant at the 0.01 level (2-tailed).

Table III (b): Correlation of Hb% with LVMI in male and female

		Hb%	LVMI female	LVMI male
Hb%	Pearson correlation	1	-0.746**	-0.778**
	Sig. (2-tailed)		0.001	0.000
LVMI grading for female	N	50	18	32
	Pearson correlation	-0.746**	1	a
LVMI grading for male	Sig. (2-tailed)	0.001		
	N	18	18	0
	Pearson correlation	-0.778**	a	1
	Sig. (2-tailed)	0.000		
	N	32	0	32

** Correlation is significant at the 0.01 level (2-tailed).

a. Cannot be computed because at least one of the variables is constant.

Discussion :

In our study, we included 50 cases of known chronic kidney disease. The percentage of female in the study group was 36 and male was 64. As female patients has less access to advanced health care facility in study, number of female are less. LVH was measured by echocardiography. Around 60% of the patients in this study had increased left ventricular mass on echocardiography. The limit for LVH for females was >112 gm/m^2. 20% of the female cases had increased left ventricular mass (Table 1). The cut-off for left ventricular hypertrophy in males was > 130 gm/m^2. 49% of the male cases had increased left ventricular mass according to Devereux formula.[7] In our study, there is association male groups had increased left ventricular mass. More patients with severe left ventricular hypertrophy were found in stage 5 of CKD in female and male which was 8 and 23 respectively. A Chronic Kidney Disease Japan Cohort (CKD-JAC) study showed LVMI increased with the stage of CKD (p=0.0005 in men, p=0.0016 in women). The prevalence of LVH was higher among patients with more advanced CKD stages. Men had a higher prevalence of LVH than women (25.1 vs. 20.6%).[13]

Previous studies shown that the prevalence of LVH is higher in CKD patients and tends to increase with the progression of CKD, especially in ESRD patients.[14-16] following is a potential explanation for how LVH accelerates the rate of eGFR decline and causes ESRD ; 1. One of the predominant causes of LVH is hypertension, as it can leads to constriction of the renal arteries, afferent arterioles, and efferent arterioles and alter the glomerular membrane filtration coefficient and tubular reabsorption. 2. Long term LVH can induce left ventricular dysfunction and decrease blood perfusion in the glomeruli, resulting in renal ischemia. 3. the associated inflammatory response, indicated by elevated plasma levels of high sensitivity C-reactive protein and interleukin 6, may contribute to and accelerate the progression of systolic dysfunction and cause rapid progression of CKD.[17]

Regarding this study, correlation of Hb% with LVMI there was a significant negative correlation was found (r= -0.420, p =0.003) between them means if Hb% decrease LVMI increases. In the study by Jesuorobo et al the hemoglobin levels of the study population had a negative correlation with left ventricular mass index and it was statistically significant.[18]

So, in Bangladesh where resource is limited, if we diagnosed anaemia with LVH in earlier stages of CKD , we can at least halt the progression of CKD to ESRD to some extent.

Limitations :

- Small sample size.
- Single center study.
- Cross sectional study.

Conclusion : Severity of anemia significantly influence the left ventricular wall thickness in chronic kidney disease patients. These predictors of left ventricular mass are very sensitive and specific for the same and are easily assessed. To increase the patients chance of surviving fatal cardiovascular conditions, strict steps should be taken to treat anemia with EPO, iron therapy, or both, and blood transfusions when there is a suspicion of probable left ventricular hypertrophy.

Recommendation

Further study with large population at multiple centers is required to improve multiple aspects of CKD management, including early diagnosis and treatment of anemia with LVH. Periodic screening and intervention for LVH and anemia in CKD patients should be practiced to prevent its complication.

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References:

1. Maqbool S, Shafiq S, Ali S, Rehman MEU, Malik J, Lee KY. Left Ventricular Hypertrophy (LVH) and Left Ventricular Geometric Patterns in Patients with Chronic Kidney Disease (CKD) Stage 2-5 With Preserved Ejection Fraction (EF): A Systematic Review to Explore CKD Stage-wise LVH Patterns. Curr Probl Cardiol. 2023 Apr;48(4):101590. doi:10.1016/j.cpcardiol.2023.101590. https://doi.org/10.1016/j.cpcardiol.2023.101590 PMid:36632930
2. R Shah, GJ Matthews, RY Shah, et al. CRIC study investigators. serum fractalkine (CX3CL1) and

cardiovascular outcomes and diabetes: findings from the chronic renal insufficiency cohort (CRIC) study. Am J Kidney Dis, 66 (2015), pp. 266-273, 10.1053/j.ajkd.2015.01.021.
https://doi.org/10.1053/j.ajkd.2015.01.021
PMid:25795074 PMCid:PMC4516570

3. N.G. Vallianou, S. Mitesh, A. Gkogkou, E. Geladari . Chronic kidney disease and cardiovascular disease: is there any relationship?. Curr Cardio Rev, 15 (2019) pp.55-63.10.2174/1573403X14666180711124825.
https://doi.org/10.2174/1573403X14666180711124825
PMid:29992892 PMCid:PMC6367692

4. R.J. Johnson, G.L. Bakris, C. Borghi, et al.Hyperuricemia, acute and chronic kidney disease, hypertension, and cardiovascular disease: report of a scientific workshop organized by the national kidney foundation. Am J Kidney Dis, 72 (2018), pp. 851-865.10.1053/j.ajkd.2017.12.009
https://doi.org/10.1053/j.ajkd.2017.12.009
PMid:29496260 PMCid:PMC7286363

5. D. Charytan. left ventricular hypertrophy a modifiable risk factor in end-stage renal disease. Curr Opin Nephrol Hypertens, 23 (2014), pp. 578-585.
https://doi.org/10.1097/MNH.0000000000000067
PMid:25295959 PMCid:PMC4266593

6. Gupta J, Dominic EA, Fink JC, Ojo AO, Barrows IR, Reilly MP, Townsend RR, Joffe MM, Rosas SE, Wolman M, Patel SS, Keane MG, Feldman HI, Kusek JW, Raj DS. Association between inflammation and cardiac geometry in chronic kidney disease : findings from the CRIC study. PLoS One. 2015; 10e124772.
https://doi.org/10.1371/journal.pone.0124772
PMid:25909952 PMCid:PMC4409366

7. Meena OP et al. A study on correlation of anaemia with left ventricular hypertrophy in chronic kidney disease patients: a cross sectional study from Southern Rajasthan, Int J Adv Med. 2022 jul; 9(7): 796-800.
https://doi.org/10.18203/2349-3933.ijam20221706

8. Journal O, Society I. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic kidney disease. 2013; 3 (1).

9. CKD DOF, Graded N. Chapter. 1: definition and classification of CKD. Kidney Int Suppl. 2013; 3 (1): 19-62.
https://doi.org/10.1038/kisup.2012.64
PMid:25018975 PMCid:PMC4089693

10. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber qualification by echocardiography in adults: an update from the American society of echocardiography and the Europian association of cardiovascular imaging. 2015; 16(3): 233-271.
https://doi.org/10.1093/ehjci/jev014
PMid:25712077

11. WHO. The Global Prevalence of Anaemia in 2011. WHO. 2011. 1-48.

12. Shuwa K. Definition and classification of chronic kidney disease: a position statementfrom Kidney Disease: improving Global Outcomes (KDIGO) J EROME R OSSERT, D ICK DE Z EEUW, T HOMAS H. H OSTETTER, N ORBERT L AMERIE, CONFERENCE. Kidney Int. 2005;67:2089-2100.
https://doi.org/10.1111/j.1523-1755.2005.00365.x
PMid:15882252

13. Nitta K, Iimuro S, Imai E, Matsuo S, Makino H, Akizawa T, Watanabe T, Ohashi Y, Hishida A. Risk factors for increased left ventricular hypertrophy in patients with chronic kidney disease: findings from the CKD-JAC study. Clin Exp Nephrol. 2019 Jan;23(1):85-98. doi: 10.1007/s10157-018-1605-z. Epub 2018 Jun 27. Erratum in: Clin Exp Nephrol. 2018 Aug 9;: PMID: 29951723; PMCID: PMC6344393.
https://doi.org/10.1007/s10157-018-1605-z

14. Nitta K, Iimuro S, Imai E, Matsuo S, Makino H, Akizawa T, Watanabe T, Ohashi Y, Hishida A. Risk factors for increased left ventricular hypertrophy in patients with chronic kidney disease. Clin Exp Nephrol. 2013; 17:730-742.
https://doi.org/10.1007/s10157-012-0758-4
PMid:23318981 PMCid:PMC3824297

15. Imai E, Matsuo S, Makino H, Watanabe T, Akizawa T, Nitta K, Iimuro S, Ohashi Y, Hishida A. Chronic Kidney Disease Japan Cohort study: baseline characteristics and factors associated with causative diseases and renal function. Clin Exp Nephrol. 2010; 14:558-570.
https://doi.org/10.1007/s10157-010-0352-6
PMid:20700621

16. Bayauli MP, Lepira FB, Kayembe PK, M'Buyamba Kabangu JR. Left ventricular hypertrophy and geometry in type 2 diabetes patients with chronic kidney disease. An echocardiographic study. Cardiovasc J Afr. 2012; 23:73-77
https://doi.org/10.5830/CVJA-2011-028
PMid:22447475 PMCid:PMC3721939

17. Gupta J, Dominic EA, Fink JC, Ojo AO, Barrows IR, Reilly MP, Townsend RR, Joffe MM, Rosas SE, Wolman M, Patel SS, Keane MG, Feldman HI, Kusek JW, Raj DS. Association between inflammation and cardiac geometry in chronic kidney disease: findings from the CRIC study. PLoS One. 2015; 10:e124772.
https://doi.org/10.1371/journal.pone.0124772
PMid:25909952 PMCid:PMC4409366

18. Jesuorobo DE. Left ventricular hypertrophy and its correlates in chronic kidney disease patients in a nigerian tertiary hospital. Intern J Intern Med. 2012; 1(3):11-6.